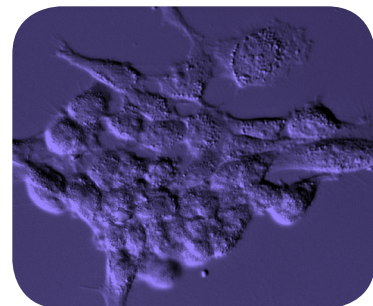




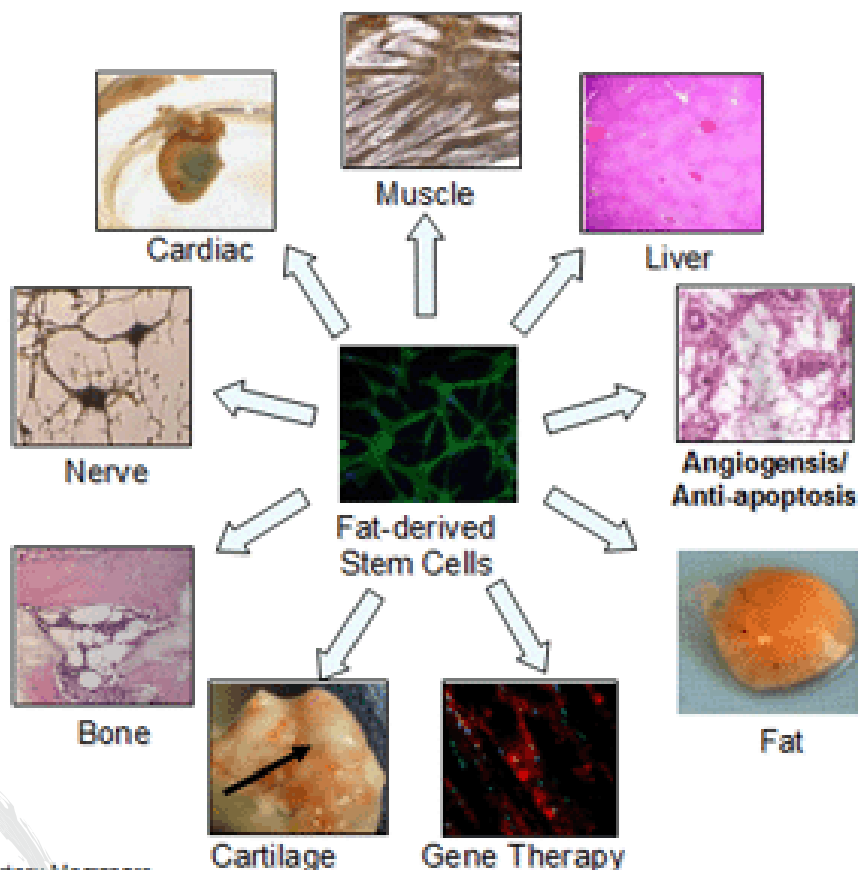
Regenerative Medicine is a broad definition for innovative medical therapies that will enable the body to repair, replace, restore and regenerate damaged or diseased tissues.

Vet-Stem Regenerative Medicine uses a concentrated form of autologous (from the patient's own tissue) adipose-derived (from body fat) adult stem cells.



## Success in human clinical trials and animal models

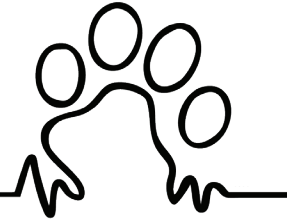
- hundreds of ongoing clinical trials
- success in clinical use veterinary medicine



**Stem cells are multipotent and can differentiate into tendon, ligament, bone, cartilage, cardiac, nerve, muscle, blood vessels, fat, and liver tissue<sup>22,23</sup> (see figure above).**

# Vet-Stem Regenerative Medicine

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## Vet-Stem Technology: Summary

- Adipose-derived stem cells (Vet-Stem Regenerative Cells: VSRC™) – NOT EMBRYONIC
- Autologous cell therapy – PATIENT's own tissue
- Currently proven and most used in dogs with osteoarthritis and for healing of bone, tendons, muscle and ligaments
- Benefits reported with immune-mediated disease, inflammatory bowel disease, kidney disease
- Under research for use in stroke, plus kidney & neurologic disease
- More than 3,500 dogs treated since 2006 (this figure is probably old, and MUCH larger now)
- No systemic adverse events reported and < 0.5% local tissue reactions.<sup>3-6</sup>

## Why use adipose-derived regenerative cells rather than regenerative cells derived from bone marrow?

Adipose-derived regenerative cells are:

- Readily available source
- Can be collected in far greater concentrations than those from bone marrow<sup>24</sup>
- Able to differentiate into multiple lineages
- Fractions isolated from adipose tissue contain a heterogeneous mixture of regenerative cells, including:<sup>23</sup>
  - o Mesenchymal stem cells (MSCs)
  - o Endothelial progenitor cells
  - o Pericytes
  - o Immune cells
  - o Fibroblasts
  - o Other growth factor-secreting bioactive cells

## Differences in Regenerative Medicine compared to traditional medicine:

- Does not rely on a single target receptor or a single pathway for its action
- Regenerative cell mixture is delivered either directly to the traumatic wound (e.g.: tendonitis, desmitis, fracture) or are delivered systemically (IV; e.g.: multifocal arthritis, renal disease)
- Regenerative cells can differentiate into many tissue types, induce repair, and stimulate regeneration<sup>22</sup>
- Regenerative cells "communicate" with the cells of their local environment, creating the optimal environment for natural healing<sup>25</sup>
- Regenerative cells produce a variety of substances that regulate tissue growth, integrity, and function<sup>25</sup>

## Mechanisms for success...

- **Anti-inflammatory/immunomodulation:**  
limit inflammatory responses and promote anti-inflammatory pathways.
- **Trophic Support:**  
secrete cytokines and growth factors that support angiogenesis (blood vessel growth), tissue remodeling, differentiation, and anti-apoptotic (preventing cell death) events.
- **Differentiation:**  
Adipose derived MSC studies demonstrate a diverse plasticity, including differentiation into adipo- (fat), osteo- (bone), chondro- (cartilage), myo- (body muscle), cardiomyo- (heart muscle), endothelial (blood vessel lining), hepato- (liver), neuro- (nerve), epithelial (skin and tissue linings) and hematopoietic (blood cell generating) lineages, similar to that described for bone marrow derived MSC.
- **Homing:**  
Homing (chemotaxis) is an event by which a cell migrates from one area of the body to a distant site where it may be needed for a given physiological event. Homing is an important function of MSCs and other progenitor cells and one mechanism by which intravenous or parenteral administration of MSCs permits an auto-transplanted therapeutic cell to effectively target a specific area of pathology. This can be used to treat infarctions (blood vessel occlusion, such as stroke), fractures, and osteoarthritis, etc.
- **Revascularization:**  
Development of and increasing numbers of blood vessels to maximize blood supply and healing. Recovery from ischemic events (thrombosis, GDV, etc.)
- **Anti -Apoptosis:**  
Apoptosis is defined as a programmed cell death or “cell suicide”, an event that is genetically controlled<sup>35</sup> Under normal conditions, apoptosis determines the lifespan and coordinated removal of cells. Unlike necrosis, apoptotic cells are typically intact during their removal (phagocytosis).
- **Central analgesia:**  
Stem cells occupy or activate opioid (morphine class) receptors in the spinal cord, providing several months of pain relief, comparable to level achieved via epidural.

### Stem Cell Therapy

Harvest at least 30-60 grams of fat

FedEx to Vet-Stem, receive dose(s) of stem cells for local or IV use within 48 hours

Inject via IV catheter and/or into joint or other site under light anesthesia

Outpatient treatment

Follow-up doses via IV injection every 9-12 months to maintain therapeutic effects.

### Stem Cell banking (StemInsure)

Harvest 5-10 grams of fat

Sent to Vet-Stem and banked for future use

Culturing takes 4-6 weeks when ready to use, can obtain virtually limitless doses over time.

**Only contraindication to treatment at this time is cancer, as effects of the stem cells on cancer cells is still being evaluated.**

